



RESPONSE TO COMMENT ON KELLY ET AL.

Subclinical First Trimester Renal Abnormalities Are Associated With Preeclampsia in Normoalbuminuric Women With Type 1 Diabetes.

Diabetes Care 2018;41:120–127

Diabetes Care 2018;41:e102–e103 | <https://doi.org/10.2337/dci18-0006>

Clare B. Kelly,^{1,2}
Michelle B. Hookham,^{1,3}
Jeremy Y. Yu,^{1,2} Alicia J. Jenkins,^{2,4}
Alison J. Nankervis,⁵
Kristian F. Hanssen,^{6,7} Satish K. Garg,⁸
James A. Scardo,⁹
Samar M. Hammad,¹⁰
M. Kathryn Menard,¹¹
Christopher E. Aston,¹² and
Timothy J. Lyons^{1,2}

We thank Foussard et al. (1) for their interest in our study (2). We agree that caution is required when identifying predictive markers of clinical interest in pregnant women with diabetes with regard to preeclampsia (PE). Accurate estimation of renal function is critical for the care of pregnant patients. Alper et al. (3) highlighted the limitations of currently available formulas for accurately predicting the glomerular filtration rate (GFR) in patients with PE. Our study focused on markers of renal function early in pregnancy prior to the clinical onset of PE.

We studied a population with type 1 diabetes, thus at high risk of PE, starting at the first trimester. We did not have preconception data and recognize that GFR can increase by up to 25% during the first trimester of a normal pregnancy (4) and that data in type 1 diabetes are lacking. We excluded women with microalbuminuria and/or hypertension at baseline (12 weeks' gestation). Not previously reported, but consistent with their elevated estimated GFR, serum creatinine was lower at ~12 weeks' (51.6 ± 5.9 vs.

56.2 ± 6.9 μmol/L, $P = 0.02$) and ~22 weeks' (50.7 ± 5.5 vs. 55.3 ± 8.5 μmol/L, $P = 0.04$) gestation in women with type 1 diabetes who later developed PE versus those who did not, but it did not differ between these groups at 32 weeks' gestation (54.5 ± 7.9 vs. 56.0 ± 8.0 μmol/L, $P = 0.53$).

In contrast, Foussard et al. (1) found higher serum creatinine at 25 weeks' gestation in seven women with gestational diabetes mellitus (GDM) who later developed PE versus the 90 women who did not. Clearly, the two cohorts are different in terms of size, type of dysglycemia, and incidence of PE. Furthermore, neither the renal nor the hypertension status of the GDM cohort, either preconception or earlier in pregnancy, is presented, and possibly the GDM women were further advanced in the evolution of subclinical renal disease than our type 1 diabetes cohort (in whom any clinically evident renal dysfunction was an exclusion).

We fully agree that confirmatory studies will be essential before any of these findings can be translated to clinical use,

but we consider that they provide important clues to underlying reasons for susceptibility to PE in women with diabetes.

Funding. This work was supported by research grants from JDRF (JDRF 1-2001-844) to T.J.L. and by the National Institutes of Health (National Center for Research Resources) grants M01-RR-1070 and M01-RR-14467 to the General Clinical Research Centers at the Medical University of South Carolina and to the University of Oklahoma Health Sciences Center, respectively.

The sponsors had no role in the design and conduct of the study; collection, management, analysis, or interpretation of the data; preparation, review, or approval of the manuscript; or decision to submit the manuscript for publication.

Duality of Interest. This work was supported by a research grant from Novo Nordisk to T.J.L., which enabled the participation of the Barbara Davis Diabetes Center for Childhood Diabetes at the University of Colorado. No other potential conflicts of interest relevant to this article were reported.

References

1. Foussard N, Coughard-Gregoire A, Rajaobelina K, et al. Comment on Kelly et al. Subclinical first trimester renal abnormalities are associated with preeclampsia in normoalbuminuric women with

¹Centre for Experimental Medicine, Queen's University Belfast, Belfast, Northern Ireland, U.K.

²Division of Endocrinology, Medical University of South Carolina, Charleston, SC

³The Department of Clinical Biochemistry, Royal Victoria Hospital, Belfast, Northern Ireland, U.K.

⁴National Health and Medical Research Council Clinical Trials Centre, University of Sydney, Camperdown, Sydney, New South Wales, Australia

⁵Diabetes Service, The Royal Women's Hospital, Melbourne, Victoria, Australia

⁶Department of Endocrinology, Oslo University Hospital, Oslo, Norway

⁷Institute of Clinical Medicine, University of Oslo, Oslo, Norway

⁸Barbara Davis Center for Childhood Diabetes, University of Colorado, Denver, CO

⁹Spartanburg Regional Medical Center, Spartanburg, SC

¹⁰Department of Regenerative Medicine and Cell Biology, Medical University of South Carolina, Charleston, SC

¹¹Division of Materno-Fetal Medicine, University of North Carolina, Chapel Hill, NC

¹²Department of Pediatrics, University of Oklahoma Health Sciences Center, Oklahoma City, OK

Corresponding author: Timothy J. Lyons, lyonstj@muscc.edu.

C.B.K. and M.B.H. contributed equally to this response.

© 2018 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. More information is available at <http://www.diabetesjournals.org/content/license>.

type 1 diabetes. *Diabetes Care* 2018;41:120–127 (Letter). *Diabetes Care* 2018;41:e101. DOI: 10.2337/dc18-0069

2. Kelly CB, Hookham MB, Yu JY, et al. Subclinical first trimester renal abnormalities are associated

with preeclampsia in normoalbuminuric women with type 1 diabetes. *Diabetes Care* 2018;41:120–127

3. Alper AB, Yi Y, Rahman M, et al. Performance of estimated glomerular filtration rate prediction

equations in preeclamptic patients. *Am J Perinatol* 2011;28:425–430

4. Hussein W, Lafayette RA. Renal function in normal and disordered pregnancy. *Curr Opin Nephrol Hypertens* 2014;23:46–53